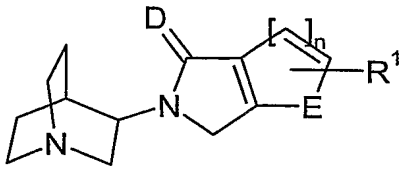
CLAIMS

1. A compound in accord with formula I:



I

wherein:

D represents O;

E represents CH_2, NH, O or S;

n is 1 or 2 and

R^1 is selected from hydrogen, halogen or a substituted or unsubstituted 5- or 6-membered aromatic or heteroaromatic ring having 0, 1 or 2 nitrogen atoms, 0 or 1 oxygen atoms, and 0 or 1 sulfur atoms, or selected from a substituted or unsubstituted 8-, 9- or 10-membered fused aromatic or heteroaromatic ring system having 0, 1, 2 or 3 nitrogen atoms, 0 or 1 oxygen atoms, and 0 or 1 sulfur atoms, said aromatic or heteroaromatic rings or ring systems, when substituted, having substituents selected from -C_1-C_6alkyl, -C_3-C_6cycloalkyl, -C_1-C_6alkoxy, -C_2-C_6alkenyl, -C_2-C_6alkynyl, halogen, -CN, -NO_2, -CF_3, -$S(O)_mR^2$ wherein m is 0, 1 or 2, -NR^2R^3, -$NR^2C(O)R^3$, -$CH_2NR^2R^3$,OR^2, -CH_2OR^2, -$C(O)NR^2R^3$, or -CO_2R^4;

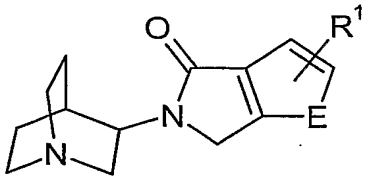
R^2 and R^3 are independently selected at each occurrence from hydrogen, -C_1-C_4alkyl, -C_1-C_4alkoxy, -C_3-C_6cycloalkyl, aryl, heteroaryl, -$C(O)R^4$, -CO_2R^4 or -SO_2R^4, or

R^2 and R^3 in combination is -$(CH_2)_jG(CH_2)_k$- or -$G(CH_2)_jG$- wherein G is oxygen, sulfur, NR^4, or a bond, j is 0, 1, 2, 3 or 4 and k is 0, 1, 2, 3 or 4, and

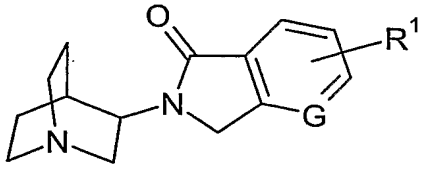
R^4 is independently selected at each occurrence from hydrogen, -C_1-C_4alkyl, aryl, or heteroaryl;

or a stereoisomer, enantiomer, *in vivo*-hydrolysable precursor or pharmaceutically-acceptable salt thereof.

2. A compound according to formula II or III:



or



II III

wherein:

E represents or CH_2, NH, O or S;

G represents CH or N;

R^1 is selected from hydrogen, halogen or a substituted or unsubstituted 5- or 6-membered aromatic or heteroaromatic ring having 0, 1 or 2 nitrogen atoms, 0 or 1 oxygen atoms, and 0 or 1 sulfur atoms, or selected from a substituted or unsubstituted 8-, 9- or 10-membered fused aromatic or heteroaromatic ring system having 0, 1, 2 or 3 nitrogen atoms, 0 or 1 oxygen atoms, and 0 or 1 sulfur atoms, said aromatic or heteroaromatic rings or ring systems, when substituted, having substituents selected from -C_1-C_6alkyl, -C_3-C_6cycloalkyl, -C_1-C_6alkoxy, -C_2-C_6alkenyl, -C_2-C_6alkynyl, halogen, -CN, -NO_2, -CF_3, -$S(O)_mR^2$ wherein m is 0, 1 or 2, -NR^2R^3, -$NR^2(CO)R^3$, -$CH_2NR^2R^3$, OR^2, -CH_2OR^2, -$C(O)NR^2R^3$, or -CO_2R^4;

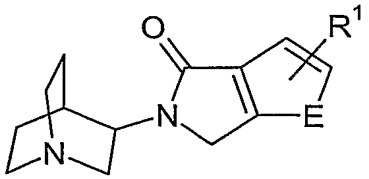
R^2 and R^3 are independently selected at each occurrence from hydrogen, -C_1-C_4alkyl, -C_1-C_4alkoxy, -C_3-C_6cycloalkyl, aryl, heteroaryl, -$C(O)R^4$, -CO_2R^4 or -SO_2R^4, or

R^2 and R^3 in combination is -$(CH_2)_jG(CH_2)_k$- or -$G(CH_2)_jG$- wherein G is oxygen, sulfur, NR^4, or a bond, j is 0, 1, 2, 3 or 4 and k is 0, 1, 2, 3 or 4, and

R^4 is independently selected at each occurrence from hydrogen, -C_1-C_4alkyl, aryl, or heteroaryl;

or a stereoisomer, enantiomer, *in vivo*-hydrolysable precursor or pharmaceutically-acceptable salt thereof.

3. A compound according to claim 1, in accord with formula II:



II

wherein:

E represents or CH_2, NH, O or S;

R^1 is selected from hydrogen, halogen or a substituted or unsubstituted 5- or 6-membered aromatic or heteroaromatic ring having 0, 1 or 2 nitrogen atoms, 0 or 1 oxygen atoms, and 0 or 1 sulfur atoms, or selected from a substituted or unsubstituted 8-, 9- or 10-membered fused aromatic or heteroaromatic ring system having 0, 1, 2 or 3 nitrogen atoms, 0 or 1 oxygen atoms, and 0 or 1 sulfur atoms, said aromatic or heteroaromatic rings or ring systems, when substituted, having substituents selected from -C_1-C_6alkyl, -C_3-C_6cycloalkyl, -C_1-C_6alkoxy, -C_2-C_6alkenyl, -C_2-C_6alkynyl, halogen, -CN, -NO_2, -CF_3, -$S(O)_mR^2$ wherein m is 0, 1 or 2, -NR^2R^3, -$NR^2(CO)R^3$, -$CH_2NR^2R^3$, OR^2, -CH_2OR^2, -$C(O)NR^2R^3$, or -CO_2R^4;

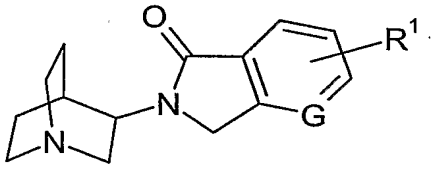
R^2 and R^3 are independently selected at each occurrence from hydrogen, -C_1-C_4alkyl, -C_1-C_4alkoxy, -C_3-C_6cycloalkyl, aryl, heteroaryl, -$C(O)R^4$, -CO_2R^4 or -SO_2R^4, or

R^2 and R^3 in combination is -$(CH_2)_jG(CH_2)_k$- or -$G(CH_2)_jG$- wherein G is oxygen, sulfur, NR^4, or a bond, j is 0, 1, 2, 3 or 4 and k is 0, 1, 2, 3 or 4, and

R^4 is independently selected at each occurrence from hydrogen, -C_1-C_4alkyl, aryl, or heteroaryl;

or a stereoisomer, enantiomer, *in vivo*-hydrolysable precursor or pharmaceutically-acceptable salt thereof.

4. A compounds according to claim 2, in accord with formula III:



III

wherein:

G represents CH or N;

R^1 is selected from hydrogen, halogen or a substituted or unsubstituted 5- or 6-membered aromatic or heteroaromatic ring having 0, 1 or 2 nitrogen atoms, 0 or 1 oxygen atoms, and 0 or 1 sulfur atoms, or selected from a substituted or unsubstituted 8-, 9- or 10-membered fused aromatic or heteroaromatic ring system having 0, 1, 2 or 3 nitrogen atoms, 0 or 1 oxygen atoms, and 0 or 1 sulfur atoms, said aromatic or heteroaromatic rings or ring systems, when substituted, having substituents selected from -C_1-C_6alkyl, -C_3-C_6cycloalkyl,

-C_1-C_6alkoxy, -C_2-C_6alkenyl, -C_2-C_6alkynyl, halogen, -CN, -NO_2, -CF_3, -$S(O)_mR^2$ wherein m is 0, 1 or 2, -NR^2R^3, -$NR^2(CO)R^3$, -$CH_2NR^2R^3$, OR^2, -CH_2OR^2, -$C(O)NR^2R^3$, or -CO_2R^4;

R^2 and R^3 are independently selected at each occurrence from hydrogen, -C_1-C_4alkyl, -C_1-C_4alkoxy, -C_3-C_6cycloalkyl, aryl, heteroaryl, -$C(O)R^4$, -CO_2R^4 or -SO_2R^4, or

R^2 and R^3 in combination is -$(CH_2)_jG(CH_2)_k$- or -$G(CH_2)_jG$- wherein G is oxygen, sulfur, NR^4, or a bond, j is 0, 1, 2, 3 or 4 and k is 0, 1, 2, 3 or 4, and

R^4 is independently selected at each occurrence from hydrogen, -C_1-C_4alkyl, aryl, or heteroaryl;

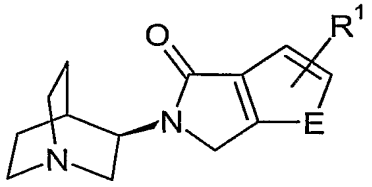
or a stereoisomer, enantiomer, *in vivo*-hydrolysable precursor or pharmaceutically-acceptable salt thereof.

5. A compound according to claim 3 or 4, wherein,

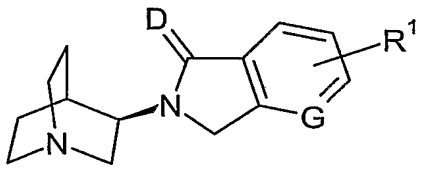
R^1 is selected from hydrogen, halogen and substituted or unsubstituted phenyl, pyridyl, quinolinyl, piperazinyl or morpholinyl, said phenyl, pyridyl, quinolinyl, piperazinyl or morpholiny, when substituted, having substituents selected from -C_1-C_6alkyl, -C_3-C_6cycloalkyl, -C_1-C_6alkoxy, -C_2-C_6alkenyl, -C_2-C_6alkynyl, halogen, -CN, -NO_2, -CF_3, -$S(O)_mR^2$ wherein m is 0, 1 or 2, -NR^2R^3, -$CH_2NR^2R^3$, -OR^2, -CH_2OR^2 or -CO_2R^4.

6. A compound according to claim 2, wherein:

said compound is an R-stereoisomer in accord with formula IV or V,



or



IV V.

7. A compound selected from:

2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-6-phenyl-2,3-dihydro-isoindol-1-one;

2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-5-(4-methyl-piperazin-1-yl)-2,3-dihydro-isoindol-1-one;

5-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-2-phenyl-5,6-dihydro-furo[2,3-*c*]pyrrol-4-one;

2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-6-bromo-2,3-dihydro-isoindol-1-one;

2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-6-pyridin-3-yl-2,3-dihydro-isoindol-1-one;

2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-6-pyridin-4-yl-2,3-dihydro-isoindol-1-one;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-5-bromo-2,3-dihydro-isoindol-1-one;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-5-phenyl-2,3-dihydro-isoindol-1-one;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-5-pyridin-3-yl-2,3-dihydro-isoindol-1-one;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-5-pyridin-4-yl-2,3-dihydro-isoindol-1-one;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-4-bromo-2,3-dihydro-isoindol-1-one;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-4-phenyl-2,3-dihydro-isoindol-1-one;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-4-pyridin-3-yl-2,3-dihydro-isoindol-1-one;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-4-pyridin-4-yl-2,3-dihydro-isoindol-1-one;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-7-bromo-2,3-dihydro-isoindol-1-one;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-7-phenyl-2,3-dihydro-isoindol-1-one;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-7-pyridin-3-yl-2,3-dihydro-isoindol-1-one;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-7-pyridin-4-yl-2,3-dihydro-isoindol-1-one;
(R)-2-(1-Aza-bicyclo[2.2.2]oct-3-yl)-2,3-dihydro-isoindol-1-one;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-5-(4-methyl-piperazin-1-yl)-2,3-dihydro-isoindol-1-one;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-5-morpholin-4-yl-2,3-dihydro-isoindol-1-one;
5-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-2-bromo-5,6-dihydro-furo[2,3-*c*]pyrrol-4-one;
5-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-2-phenyl-5,6-dihydro-furo[2,3-*c*]pyrrol-4-one;
5-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-2-pyridin-3-yl-5,6-dihydro-furo[2,3-*c*]pyrrol-4-one;
5-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-2-pyridin-4-yl-5,6-dihydro-furo[2,3-*c*]pyrrol-4-one;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-6-(3-chloro-phenyl)-2,3-dihydro-isoindol-1-one;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-6-(4-chloro-phenyl)-2,3-dihydro-isoindol-1-one;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-6-quinolin-8-yl-2,3-dihydro-isoindol-1-one;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-6-benzo[1,3]dioxol-5-yl-2,3-dihydro-isoindol-1-one;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-6-(2-chloro-phenyl)-2,3-dihydro-isoindol-1-one;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-6-(2-methoxy-phenyl)-2,3-dihydro-isoindol-1-one;
N-[3-((R)-2-1-Aza-bicyclo[2.2.2]oct-3-yl-3-oxo-2,3-dihydro-1H-isoindol-5-yl)-phenyl]-acetamide;
2-(R)-1-Aza-bicyclo[2.2.2]oct-3-yl-6-morpholin-4-yl-2,3-dihydro-isoindol-1-one, or
4-((R)-2-1-Aza-bicyclo[2.2.2]oct-3-yl-3-oxo-2,3-dihydro-1H-isoindol-5-yl)-N,N-dimethyl-benzamide.

8. A compound according to Claim 1 or 2, wherein one or more of the atoms is a radioisotope of the same element.

9. A compound according to Claim 1 or 2, additionally comprising one or more atoms selected from tritium, ^{18}F, ^{123}I, ^{125}I, ^{131}I, ^{75}Br, ^{76}Br, ^{77}Br or ^{82}Br.

10. A method of treatment or prophylaxis of diseases or conditions in which activation of the α7 nicotinic receptor is beneficial which method comprises administering a therapeutically-effective amount of a compound according to Claim 1 or 2 to a subject suffering from said disease or condition.

11. The method of treatment or prophylaxis according to Claim 10, wherein the disorder is anxiety, schizophrenia, mania or manic depression.

12. A method of treatment or prophylaxis of neurological disorders, psychotic disorders or intellectual impairment disorders, which comprises administering a therapeutically effective amount of a compound according to Claim 1 to a subject suffering from said disease or condition.

13. The method of treatment or prophylaxis according to Claim 12, wherein the disorder is Alzheimer's disease, learning deficit, cognition deficit, attention deficit, memory loss, or Attention Deficit Hyperactivity Disorder.

14. The method of treatment or prophylaxis according to Claim 12, wherein the disorder is Parkinson's disease, Huntington's disease, Tourette's syndrome, or neurodegenerative disorders in which there is loss of cholinergic synapses.

15. A method of treatment or prophylaxis of jetlag, nicotine addiction, craving, pain, and for ulcerative colitis, which comprises administering a therapeutically effective amount of a compound according to Claim 1 or 2.

16. A method for inducing the cessation of smoking which comprises administering an effective amount of a compound according to Claim 1.

17. A pharmaceutical composition comprising a compound according to Claim 1 and a pharmaceutically-acceptable diluent, lubricant or carrier.

18. The use of a compound according to Claim 1, an enantiomer thereof or a pharmaceutically-acceptable salt thereof, in the manufacture of a medicament for the treatment or prophylaxis of neurological disorders, psychotic disorders or intellectual impairment disorders selected from Alzheimer's disease, learning deficit, cognition deficit, attention deficit, memory loss or Attention Deficit Hyperactivity Disorder, anxiety, schizophrenia, or mania, manic depression, Parkinson's disease, Huntington's disease, Tourette's syndrome, neurodegenerative disorders in which there is loss of cholinergic synapses, jetlag, pain, or ulcerative colitis.